Review Article

An Update in Adult Intraosseous Infusion

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Abstract

The Intraosseous (IO) needle was developed in 1920s to access the vascular system via the bone marrow cavity. Around the 2010s, there was widespread interest in IO after the American Heart Association (AHA) recommended that intraosseous access is an optional route when intravenous (IV) access cannot be obtained quickly. IO had a higher success rate (99.6%), was faster to perform (15-24 seconds), had a nearly equal flow rate (1-5L/hr), and had almost equal drug bioavailability to IV. The complication of IO becoming dislodged was 10-16%, needle dislocation was 0.8%, needle bending was 0.4% and parafusion (defined as fluid leakage at the insertion site causing tissue edema surrounding the leakage point) was 0.4%. Most retrospective trials and meta-analysis studies found that hospital discharge, return of spontaneous circulation (ROSC), and favorable neurological outcome was higher with IV than with the IO group. In conclusion, IO is still beneficial for immediate vascular access and should be placed after and/or simultaneously to IV insertion.

Objectives: to update content of adult intraosseous infusion in critical situations.

Keywords: intraosseous infusion, intraosseous access, IO, intravenous access, IV

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Introduction

The Intraosseous (IO) needle was developed in the 1920s[1] to access the vascular system via the bone marrow cavity but was decreasingly used when an intravenous needle was developed in the 1950s.[2] In the 1980s, intraosseous devices were reintroduced in combat or emergency conditions.

The Food and Drug Administration (FDA) approved the use of a manual-driven First Access for Shock and Trauma (FAST1™) device in 1997, an automatic spring-loaded impact-driven Bone Injection Gun (BIG™) in 2000 which was developed to NIO™ later, and Semi-automatic battery driven EZ-IO™ in 2004.[2] Around the 2010s, there was wide interest in IO after the American Heart Association (AHA) recommended that intraosseous access is an optional route when intravenous (IV) access cannot be obtained quickly. In 2020, AHA recommended that epinephrine should be given as soon as possible in non-shockable cardiac arrest and that IO is the best possible option to achieve this.

Success rate

Overall, IO success rate was 99.6%[3] with a first attempt success rate of 85.9-94.8%,[3,4] while first attempt success rate of IV is 50-81.6%.[4,5] In addition, first-attempt success rate was 95% for proximal humerus,[6] 95% for distal femur,[6] 84-92% for proximal tibial[2,6] and 72% for sternum using FAST1™.[7,8] And there was no significant difference between EZ-IO™ and NIO™ device.[2]

Indications

- Failure of venous insertion in 2 attempts and/or taking more than 90 seconds.[9-11]
- Immediate vascular access is required.[11]

Contraindications

- Site of fracture, burn, infection, or bone diseases (e.g. bone tumor, osteoporosis, osteogenesis imperfecta).
- Recent orthopedic surgery or previous IO site.
- Lower limb in patients with severe abdominal trauma[10,11]

Procedure time

The time to perform IO was around 15-20 seconds for EZ-IO™,[10] 17-24 seconds for BIG™/NIO™,[5,10] 20-24 seconds for manual needle,[5,10] and 50-67 seconds for FAST1™.[8,10]

Complications

Minor complications: dislodged IO rate was 16% for the proximal humerus, 10% for the distal femur, and 15% for the proximal tibia.[6] Needle dislocation was 0.8%, needle bending was 0.4% and parafusion was 0.4%.[3] Severe complications: fat emboli after IO insertion were not different from the non-IO group, and only CPR could cause emboli in animal studies.[12] Bone damage was observed in animal studies and found that metaphyseal bone was completely resolved at 3 weeks and complete epiphyseal closure at 6 months.[12]

Flow rate

Generally, the flow rate was 5 L/hr in the proximal humerus and 1L/hr in the proximal tibia.[6,10] However, cadaveric and critical human studies showed that the gravity flow rate was around 3 L/hr in sternal IO (SIO),[13] 2.4 L/hr in humeral IO (HIO),[13,14] and 1.8 L/hr in tibial IO (TIO).[13,14] Under 300 mm Hg pressure flow rate was around 3.6-9.6 L/hr in SIO,[13] 4.8-6 L/hr in HIO,[13,14] and 3-7.2 L/hr in TIO.[13,14]

Pharmacokinetic studies

The systematic review found that in non-cardiac arrest animal studies, IO had an equivalent bioavailability (area under the curve of plasma concentration (AUC)), maximum plasma concentration (C_{max}), and time to maximum plasma concentration (T_{max}) compared to IV administration for many drugs such as epinephrine, atropine, sodium bicarbonate, dextrose 50%, and calcium chloride.[12]

Mostly hypovolemic cardiac arrest animal studies found no statistically significant differences between IO groups (SIO,[15] HIO,[16,17] TIO[18]) and IV groups in C_{max} or T_{max}, but lower C_{max} in IO groups and longer T_{max} in IO groups,[15,16,18] such as lower C_{max} in the TIO group 56,292 ± 11,504 ng/mL compared to 74,258 ± 11,504 ng/mL in the IV group ($p = 0.291$), and longer T_{max} in the TIO group 120 ± 25 seconds compared to 94 ± 25 seconds in the IV group ($p = 0.475$).[18]

But one normovolemic cardiac arrest study found that C_{max} in the IV group was equal to both

HIO (p = 0.33) and TIO groups (p = 0.060), but C_{max} in the HIO group was higher than the TIO group (p = 0.007). The T_{max} in the IV group was equal to the HIO group (p = 0.328), but T_{max} in both IV and HIO groups were shorter than TIO group (p < 0.05).[17]

Location

- Sternum: 1 cm below the sternal notch (with FAST1™ only).
- Proximal humerus: The humerus should be internally rotated, the elbow flexed to 90 degrees, and the hand should be placed on the abdomen. Then the needle (length > 45 mm) is inserted 2 cm above the surgical neck at 45 degrees pointing to the contralateral hip.
- Distal femur: With the leg straightened and centered in the anterior plane, 1 cm proximal to the patella, and 1 to 2 cm medially.
- Proximal tibia: 1 cm to 2 cm inferomedial to the tibial tuberosity in the center of the tibia.
- Distal tibia: 2 cm proximal to the medial malleolus in the center of the tibia.[11]

A retrospective CT/MRI study found that the proper insertion depth was 26.0-56.5 mm in males and 27.5-52.5 mm in females for the proximal humerus, 20.5-42.0 mm in males and 32.5-45.5 mm in females for proximal tibia, and 16.5-34.5 mm in males and 14.5-30.5 mm in females for distal tibia. Females had a thicker soft tissue cover (+7.8 mm, 95% CI 3.7-10.1, p < 0.01) in the proximal tibia. Although, all 3 sites did not have gender-specific differences in the IO insertion depth.[19]

Technique

- When the needle passes through the cortical bone, loss of resistance is felt, the tip of the needle is in bone marrow cavity.
- Confirm the position of the IO needle by checking for the stability of the needle in the bone, and the ability to flush with saline, without extravasation.[11]
- For conscious patients, 20-40 mg (epinephrine-free, preservative-free) lidocaine is slowly injected through the IO catheter to relieve flush pain. And wait 2 minutes for the lidocaine effect before flushing.[11,20]
- Some studies recommended using an infusion pump or pressure bag for persistent, continuous flow[10,20] and stabilizer dressings with restricted ambulation to prevent IO dislodement.[20]

Duration

- US FDA recommended to use IO not more than 24 hrs, but could be extended to 48 hrs if IV access is not available.[11,20]
- One stable co-morbidities patients study found no serious adverse events up to 30 days-follow up, after 48 hrs IO insertion in both proximal humerus and proximal tibia. Although it had a limitation of using normal saline infusion only.[20]

Lab

- Systematic review showed that evidence on the agreement between IO and the arterial or venous sample was weak due to improper statistical analysis (recommended using the Bland-Altman method), and small sample size.[21]
- A small study of 17 CPR patients found that IO and IV samples were most comparable for sodium bicarbonate, base excess and pH. In addition, intraclass correlation coefficients were excellent for sodium.[22]

Clinical outcome

In normo-hypovolemic cardiac arrest animal studies found that no statistical difference in ROSC for SIO vs IV (p = 0.191),[15] HIO vs IV (p = 1),[16] or HIO vs TIO vs IV (p > 0.05)[17] and time to ROSC for SIO vs IV (p > 0.05),[15] or HIO vs IV (p = 0.22).[16]

In a retrospective study, overall ROSC is the same in all 3 IO sites by proximal humerus 36.3% (95% CI 32.6-40.6), distal femur 30.3% (95% CI 27.3-33.4), and proximal tibia 29.2% (95% CI 25.5-33.2).[6]

An APLS trial found that discharge survival was significantly higher in recipients of IV amiodarone (RR 1.26, 95% CI 1.06-1.50); absolute survival difference 5.5% (95% CI 1.5-9.5) and IV lidocaine (RR 1.21, 95% CI 1.02-1.45); absolute survival difference 4.7% (95% CI 0.7-8.8), but not in recipients of IO amiodarone (RR 0.94, 95% CI 0.66-1.32) or IO lidocaine (RR1.03, 95% CI 0.74-1.44). A limitation of this study was the route of administration

was not randomized, but drugs were randomized (amiodarone: lidocaine: placebo = 1:1:1). This trial suggested that both drug outcomes were better in the IV group.[23]

A retrospective study found that IO group was not associated with survival to discharge (OR 0.81, 95% CI 0.55-1.21, p = 0.31), but was associated with a lower likelihood of ROSC (OR 0.67, 95% CI 0.50-0.88, p = 0.004) and survival to hospital admission (OR 0.68, 95% CI 0.51-0.91, p = 0.009).[24] Multivariable adjusted OR between IO access and outcome were similar to the results from the overall cohort when the vascular access interval was included in the model for survival to discharge (OR 0.87, 95% CI 0.54-1.40, p = 0.56) and ROSC (OR 0.69, 95% CI 0.50-0.95, p = 0.02), although survival to hospital admission was no longer statistically significant (OR 0.72, 95% CI 0.51-1.01, p = 0.06).[24]

A secondary analysis of the PRIMED study found that intraosseous access was associated with poorer out-of-hospital cardiac arrest survival compared to IV (OR 0.24, 95% CI 0.12-0.46) and lower favorable neurological outcomes than IV (1.5% vs 7.6%). Sensitivity analyses revealed similar results by using the propensity score to adjust the probability of vascular access type.[25]

Meta-analysis suggested no significant association between the favorable neurological outcome and types of vascular access (OR 0.60, 95% CI 0.27-1.33, I^2 95%), but had a trend to favor IV in short-term survival (OR 0.71, 95% CI 0.59-0.85, I^2 86.45), and survival to hospital discharge (OR 0.66, 95% CI 0.42-1.04, I^2 88.75).[26]

The subgroup analyses found that time to intervention might be a significant outcome moderator. For example, the favorable neurological outcome, if the studies were not adjusted with time to intervention, the heterogeneity extensively decreased, and IO access was inversely associated with favorable neurological outcome (OR 0.22, 95% CI 0.17-0.30, I^2 0%).[26]

Another meta-analysis suggested that pooled results from four adult observational studies favored IV access with very low certainty of evidence in favorable neurological outcomes (OR 0.60, 95% CI 0.52-0.69, I^2 89), ROSC (OR 0.72, 95% CI 0.68-0.76, I^2 57) and survival to hospital discharge (OR 0.71, 95% CI 0.63-0.79, I^2 71).[27] And time to drug administration led to resuscitation time bias in observational studies.[26,27]

Simulation training

In a crossover randomized simulation study,[1] 75 novice physicians were trained only one time to IO access with BIG™ Pediatric, EZ-IO™, NIO™ Pediatric, and Jamshidi needle. After 6 months without IO application, 68 physicians can perform IO correctly with a success rate of 100% for NIO™ Pediatric, 97% for EZ-IO™, 90% for BIG™ Pediatric, and only 43% for manual Jamshidi needle. Moreover, 3 mechanical devices had a lower procedure time than the Jamshidi needle (16-29 seconds vs 29.5-45 seconds, P < 0.001) and needle bending was found to be 57% for jamshidi needle but less than 10% with mechanical devices.[1] Finally, one simulation study suggested that training should be done more than 3 times a year but in uncommon high-risk scenarios every 6 weeks to ensure high performance throughout the year.[28]

Discussion

In the ideal, IO is equal to IV in pharmacokinetic parameters, therefore IO outcome should be equal to IV outcomes if there are the same scenarios, especially at similar duration of time to vascular access, which is supported by animal studies in normohypovolemic cardiac arrest studies.[12,15-18] However, in most retrospective[24] studies, clinical trials[23,25] and meta-analysis,[26,27] human studies found that hospital discharge, ROSC, and favorable neurological outcome in IV are higher than IO group, but these have some limitations. Especially vascular type access is not randomly assigned; and this can lead to selection bias, such as resuscitation time bias, found by meta-analysis of observational studies or non-randomized trial.[26,27] This bias can lead to the inverse outcome or dilutional effect of IO. Generally, longer vascular access leads to prolonged CPR, and poorer outcomes that are not followed by effective management such as epinephrine administration.[29] Other confounders are the site of IO and the quality of IO function that cause extensively different flow rates in these studies.[6,10,13,14] A well-designed pediatric septic shock RCT confirms that IO is superior to IV in ROSC (93.3% vs 60%, p = 0.002, power back calculation is 83) resulting from rapid vascular access in IO group (52.5 vs 90 seconds, p = 0.001)

and sensitivity analysis suggests that vascular access time had a trend to longer times in deceased group compared to the discharged group (patients in the death group had longer vascular access time than patients that were discharged from hospital) but it did not have statistical difference (75 vs 60 seconds, p = 0.881).[30] The value of IO is rapid vascular access, which leads to faster effective treatment (such as fluid or medications) resulting in better outcome.

In conclusion, intraosseous access provides rapid and reliable access to administer life-saving medications during cardiac arrest. However, IO has shown poorer neurological outcomes, ROSC and the survival outcomes compared to IV. Therefore, we suggest to insert IO after and/or simultaneously to IV insertion to improve clinical outcomes.

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